THE CLAIMS

What is claimed is:

1. A method of treating at least one bone or cartilage condition which comprises administering to an animal a therapeutically effective amount of an agent comprising creatine, or an analogue or pharmaceutically acceptable salt thereof, to treat bone or cartilage conditions.

2. The method of claim 1, wherein the animal is a mammal and the condition comprises a bone or cartilage disease, a bone fracture or defect, or a degenerative disease of cartilage.

3. The method of claim 2, wherein the mammal is a human and the disease comprises osteoporosis, osteoarthritis, or periodontitis.

4. The method of claim 2, wherein the mammal is a human and the agent is incorporated in a bone or cartilage graft that is applied to the bone fracture or defect.

5. The method of claim 4, wherein the agent is incorporated in at least one three dimensional construct of osteoblasts, chondrocytes, or mesenchymal stem cells designed for tissue engineering of the bone or cartilage condition and wherein the construct is administered to the bone or cartilage.

6. The method of claim 5, further comprising:

obtaining bone or cartilage forming cells from a healthy individual;

culturing the bone or cartilage forming cells in the presence of the agent to form a three-dimensional cell assembly; and

transferring the three-dimensional cell assembly to a specific location having a bone or cartilage defect of the patient.

7. The method of claim 1, wherein the creatine, or analogue or pharmaceutically acceptable salt thereof, comprises creatine, creatine phosphate, creatine pyruvate, cyclocreatine, homocreatine, or homocyclocreatine.

8. The method of claim 1, further comprising administering at least one of: hormones, vitamins, growth factors, cytokines, matrix proteins, serum proteins, enzymes, calcium salts, fluoride salts, bone meal, hydorxyapatite, peptides, antioxidants, transferrin, selenium, boron, silicon, or nitric oxide.

9. The method of claim 8, wherein, when administered, the hormones comprise parathyroid hormone-related protein, thyroid hormone, insulin, a sex steroid, prostaglandins, or glucocorticoids; the vitamins comprise $1,25(OH)_2$ vitamin D_3 and analogues or metabolites of vitamin D, vitamin C/ascorbate, or retinoids; the growth factors comprise insulin-like growth factors (IGF), transforming growth factor b family (TGF-b), bone morphogenic proteins (BMP), basic fibroblastic growth factor (bFGF), platelet derived growth factor (PDGF), or epidermal growth factor (EGF); the cytokines comprise interleukins (IL), interferons, or leukaemia inhibitory factor (LIF); the matrix proteins comprise collagens, glycoproteins, hyaluronan, or proteoglycans; the serum proteins comprise albumin or alpha-2H5 glycoprotein; the enzymes comprise metalloproteinases, collagenases, gelatinases, stromelysins, plasminogen activators, cysteine proteinases, or aspartic proteinases; the fluoride salts comprise sodium fluoride or monosodium fluorophosphate; the peptides comprise amylin, vasoactive agents, or neuropeptides; the antioxidants comprise cysteine, N-acetyl-cysteine, glutathions, or vitamins A, C, D, or E .

10. The method of claim 9, wherein, when matrix proteins are administered, the matrix proteins are glycoproteins comprising alkaline phosphatase, osteonectin (ON), gamma-carboxy glutamic acid-containing proteins, or arginine-glycine-asparagine-containing proteins, or proteoglycans comprising aggrecan, versican, biglycan, or decorin.

11. The method of claim 9, wherein the hormone is parathyroid hormone and the parathyroid hormone is administered intermittently with the agent.

12. The method of claim 11, further comprising administering $1,25(OH)_2$ vitamin D_3 and analogues or metabolites of vitamin D, calcitonine, estrogen, or bisphosphonates to the individual.

13. The method of claim 1, wherein the bone comprises cells comprising osteoblasts, periosteal cell, stromal bone marrow cells, satellite cells of muscle tissue, or mesenchymal stem cells, or a combination thereof.

14. The method of claim 1, wherein the cartilage comprises cells comprising chondroblasts or mesenchymal stem cells.

15. The method of claim 5, wherein the stem cells are cultured as monolayers, micromass cultures, or in a three-dimensional biodegradable scaffold.

16. The method of claim 6, wherein the three-dimensional cell assembly has a structure of a seeded sponge, foam, or membrane.

17. The method of claim 6, wherein 10 to 20 mM of creatine is concentrated in a culture medium containing one of 0.1% to 5% fetal calf serum or 10 to 250 μg of ascorbic acid or an equivalent amount of a pharmaceutically acceptable ascobate.

18. The method of claim 6, wherein a cell culture is started with 2,000 to 100,000 cells.

19. The method of claim 1, wherein the agent is essentially free of one or more of dihydrotriazine; dicyano-diamide; or creatinine.

20. The method of claim 1, wherein the agent is administered to a human patient in an amount of 1.4 to 285 mg per day.

21. The method of claim 1, wherein the creatine analogue has the general formula:

Z_1- - -C(- - -Z_2)- - -X-A-Y

and pharmaceutically acceptable salts thereof, wherein:

Y is selected from: -CO_2H, -NI-OH, -NO_2, -SO_3H, -C(=O)$NHSO_2J$, and -P(=O) (OH) (OJ), wherein J is selected from: hydrogen, C_1-C_6 straight chain alkyl, C_3-C_6 branched alkyl, C_2-C_6 straight alkenyl, C_3-C_6 branched alkenyl and aryl;

A is selected from: C, CH, C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, and C_1-C_5 alkoyl chain, each having 0-2 substituents which are selected independently from:

K, where K is selected from: C_1-C_6 straight alkyl, C_2-C_6 straight alkenyl, C_1-C_6 straight alkoyl, 3-6 branched alkyl, C_3-C_6 branched alkenyl, C_4-C_6 branched alkoyl, K having 0-2 substituents independently selected from: bromo, chloro, epoxy and acetoxy;

an aryl group selected from: a 1-2 ring carbocycle and a 1-2 ring heterocycle, wherein the aryl group contains 0-2 substituents independently selected from: -CH_2L and -$COCH_2L$, wherein L is independently selected from: bromo, chloro, epoxy and acetoxy; and

-NH-M, wherein M is selected from: hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_1-C_4 alkoyl, C_3-C_4 branched alkyl, C_3-C_4 branched alkenyl, and C_4-C_6 branched alkoyl;

X is selected from: NR_1, CHR_1, CR_1, O and 5,

wherein R_1 is selected from:

hydrogen,

K where K is defined above; and

an aryl group selected from: a 1-2 ring carbocycle and a 1-2 ring heterocycle, wherein the aryl group contains 0-2 substituents independently selected from: -CH_2L and -$COCH_2L$ where L is defined above;

a C_5-C_9 Alpha-amino-omega-methyl-omega-adenosyl carboxylic acid attached via the omega-methyl carbon;

a C_5-C_9 Alpha-amino-omega-aza-omega-methyl-omega -adenosylcarboxylic acid attached via the omega-methyl carbon; and

a C_5-C_9 Alpha-amino-omega-thia-omega-methyl-omegaadenosylcarboxylic acid wherein A and X are connected by a single or double bond;

Z_1 and Z_2 are chosen independently from: =O, -NHR_2, -CH_2R_2, -NR_2OH; wherein, Z_1 and Z_2 may not both be =O and wherein R_2 is selected from:

hydrogen;

K, where K is defined above;

an aryl group selected from: a 1-2 ring carbocycle and a 1-2 ring heterocycle, wherein the aryl group contains 0-2 substituents independently selected from: -CH_2L and -$COCH_2L$ where L is as defined above;

a C_4-C_8 Alpha-amino-carboxylic acid attached via the omega - carbon;

B, wherein B is selected from: -CO_2H, -NHOH, NO_2, -SO_3H, -C(=O)$NHSO_2J$ and -P(=O) (OH) (OJ), wherein J is as defined above:

D-E, wherein D is selected from: C_1-C_3 straight chain alkyl, C_3 branched alkyl, C_2-C_3 straight alkenyl, C_3 branched alkenyl, C_1-C_3 straight alkoyl, and aryl; and E is selected from: -$(PO_3)_n$NMP, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=0) (OCH_3) (O)]$_m$-Q, wherein m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH_2)]$_m$-Q, where m is 0-3 and Q is a ribonucleoside

connected via the ribose of the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO_2G, where G is independently selected from: C_1-C_6 straight alkyl, C_2-C_6 straight alkenyl, C_1-C_6 straight alkoyl, C_3-C_6 branched alkyl, C_1-C_6 branched alkenyl, C_4-C_6 branched alkoyl; wherein E may be attached at any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and

E, wherein E is as defined above,

provided that:

when E is aryl, B may be connected by an amide linkage;

if R_1 and at least one R_2 group are present, R_1 may be connected by a single or double bond to an R_2 group to form a cycle of 5 to 7 members;

if two R_2 groups are present, they may be connected by a single or double bond to form a cycle of 5 to 7 members; and

if R_1 is present and or Z_2 is selected from -NHR_2, -CH_2R_2 and -NR_2OH, then R_1 may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or to form a cycle of 4 to 7 members.

22. A method of promoting growth and mineralization of bone or cartilage cells and tissues which comprises administering to a subject in need of such treatment a therapeutically effective amount of an agent comprising creatine, or an analogue or pharmaceutically acceptable salt thereof, to promote growth and mineralization of bone or cartilage therein.

23. A method of improving acceptance and osseous integration of bone implants which comprises administering to a subject in need of such treatment a therapeutically effective amount of an agent comprising creatine, or an analogue or pharmaceutically acceptable salt thereof, to improve acceptance and osseous integration of bone implants.

24. A method for accelerating healing in a subject having a defect in bone or cartilage tissue caused by trauma, surgery, or a degenerative disease, which method comprises administering to the subject a therapeutically effective amount of a creatine compound, analogue or pharmaceutically acceptable salt thereof, or a creatine kinase.

25. A composition useful for the treatment of defects in bone or cartilage tissue of animals or humans caused by trauma or surgery, the composition comprising a creatine compound, analogue or pharmaceutically acceptable salt thereof, the composition being suitable for oral administration and including a pharmacologically suitable carrier to improve bioavailability.

26. The composition of claim 25, wherein the carrier is selected from: carbohydrates, maltodextrins, and dextrose.

27. A method of preparing an agent for treatment of bone or cartilage cells or tissues, comprising:

removing bone or cartilage forming cells from a healthy subject;

adding the bone or cartilage forming cells to a cell culture;

transfecting the bone or cartilage forming cells with complementary DNA coding for creatine kinase isoforms and made to overexpress creatine kinase isoenzyme(s); and

expanding and cultivating the bone or cartilage forming cells to form *in vitro* genetically engineered cartilage or bone tissues transplantable into areas of cartilage or bone defects of the healthy subject.